# AN EXPLORATORY MULTICENTER, OPEN-LABEL, SINGLE ARM STUDY OF THE SAFETY AND TOLERABILITY OF PIRFENIDONE (ESBRIET®) IN COMBINATION WITH NINTEDANIB (OFEV®) IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

Published: 19-01-2016
Last updated: 17-04-2024

Primary Safety Objective * Proportion of patients who complete 24 weeks of combination treatment on pirfenidone at a dose of 1602*2403 mg/d and nintedanib at a dose of 200*300 mg/d Secondary Safety Objective * Proportion of patients who discontinue...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Pleural disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON43469

**Source**
ToetsingOnline

**Brief title**
MA29895/ Esbriet combo study

### Condition

- Pleural disorders

**Synonym**
Idiopathic pulmonary fibrosis, pulmonary fibrosis

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Roche Nederland B.V.
**Source(s) of monetary or material Support:** Farmaceutische Industrie

## Intervention

**Keyword:** combination therapy, Idiopathic pulmonary Fibrosis, Safety, Tolerability

## Outcome measures

**Primary outcome**

EFFICACY ANALYSES

The efficacy measures of this study will only be analyzed in an exploratory

manner and are as follows:

* Change from baseline in %FVC

* Change from baseline in predicted DLco

* Observed and change values for percent predicted FVC and percent predicted

DLco will be summarized. Three summaries of FVC and DLco change values will be

provided:

* The historical value closest to 6 months (i.e. 168 days) before the start of

Screening vs the Baseline

* The Baseline value vs the data obtained during combination treatment through

Week 12

* The Baseline value vs the data obtained during combination treatment through

Week 24

SAFETY ANALYSES

Safety Measures are as follows:

* Number of patients who completed 24 weeks of combination therapy

* Frequency of TEAEs and Treatment-Emergent Serious Adverse Events (TESAEs)

* Gastrointestinal side effects

* Physical examination findings, including vital signs measurements, body

weight (kg), and body mass index (BMI)

* Clinical laboratory tests

* ECGs

* Early study treatment discontinuation, including reasons

* Deaths and cause of deaths

**Secondary outcome**

Patient-Reported Outcome Measures:

The PRO objectives for this study are as follows:

* KBILD at baseline and Week 24. The overall score and individual items are

endpoints.

# Study description

**Background summary**

Idiopathic pulmonary fibrosis (IPF) is a devastating orphan disease of unknown etiology characterized by progressively decreasing lung volume, worsening dyspnea, and diminishing exercise capacity is recognized by the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Association (LATA) as a distinct form of chronic fibrosing interstitial pneumonia. IPF occurs primarily in older adults, is limited to the lungs, and is defined by a radiologic and histopathologic pattern of usual interstitial pneumonia (UIP); it is the most

common of the UIPs.

IPF typically begins insidiously, with exertional dyspnea and nonproductive cough; the clinical course is unpredictable and ranges from slow and progressive respiratory decline to abrupt and accelerated deterioration. IPF is irreversible and ultimately fatal, with progressive disability and morbidity due to respiratory insufficiency. The diagnosis of IPF carries a bleak prognosis, with an estimated median survival after diagnosis of only 2.5 to 5 years

Although the pathogenesis of IPF remains incompletely understood, the current view is that a series of microinjuries to the alveolar epithelium results in release of profibrotic mediators, causing fibroblast and myofibroblast proliferation, organization into fibroblastic foci, and excessive collagen deposition and accumulation.

**Study objective**

Primary Safety Objective
* Proportion of patients who complete 24 weeks of combination treatment on pirfenidone at a dose of 1602*2403 mg/d and nintedanib at a dose of 200*300 mg/d

Secondary Safety Objective
* Proportion of patients who discontinue pirfenidone, nintedanib, or both study treatments because of adverse events before the Week 24 Visit
* Total number of patient days of combination treatment with pirfenidone at a dose of 1602*2403 mg/d and nintedanib at a dose of 200*300 mg/d
* Total number of days from the initiation of combination treatment to discontinuation of pirfenidone, nintedanib, or both study treatments
* Frequency and timing of Adverse (AE) and Serious Adverse Events (SAEs)

For futher objectives see protocol section 2.2 and 2.3

**Study design**

This is a multicenter, international, open-label, single-arm safety and tolerability study of pirfenidone/nintedanib combination treatment in patients with IPF who have been on a stable dose of pirfenidone with demonstrated tolerability. In this study, a stable pirfenidone dose will be defined as 1602* 2403 mg/d (801 mg BID or TID). Up to approximately 60 clinical centers in the US, Europe, and Canada are expected to enroll up to approximately 80 patients.

See further protocol section 3.1

**Intervention**

Patients will receive next to their treatment with pirfenidone a treatment of 24 weeks with nintedanib. Patients will be asked to complete a questionnaire at the beginning and the end of the study. During the whole study the patient is asked to complete a diary with adverse events, used medication and time and dose of the study medication.

**Study burden and risks**

As both study drugs have gastrointestinal side effects, it is expected that the frequency of these side effects will increase, i.e. nausea, diarrhoea, vomiting and resulting weight loss.

These expected side effects, can however, vary from mild to very serious and may vary from person to person. Everyone taking part in the study will be watched carefully for any side effects.

For more side effects see section 9 and appendix II if the patient information

# Contacts

**Public**
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL
**Scientific**
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

*Male or female, and age 40 through 80 years old ;*At the start of screening, on pirfenidone for at least 16 weeks and on a stable dose for at least 28 days (in this study, a stable dose will be defined as 1602*2403 mg/d); the dose must be expected to remain in that range throughout the study;*Documented diagnosis of IPF, per the Investigator per using the criteria of the 2011 American Thoracic Society / European Respiratory Society / Japanese Respiratory Society / Latin American Thoracic Association guidelines;*Pulmonary function test results at screening, percent predicted forced vital capacity (FVC) * 50% and percent predicted carbon monoxide diffusing capacity (DLco) * 30%;*For women of childbearing potential: agreement to remain abstinent or use two adequate methods of contraception, including at least one method with a failure rate of < 1% per year, during the treatment period and for at least 3 months after the final Follow-up Visit;*For men: agreement to remain abstinent or use contraceptive measures and agreement to refrain from donating sperm during the treatment period and for at least for at least 3 months after the final Follow-up Visit

## Exclusion criteria

- Clinical evidence of any active infection which according to the judgment of the investigator may interfere with study conduct, measurements of pulmonary function, or impact the course of the IPF;*In the 28 days before the start of screening, any new or ongoing moderate or severe adverse reaction considered by the Investigator to be related to pirfenidone, or an pirfenidone treatment interruption > 7 days for any reason;*Any condition that is likely to result in death in the 12 months after the start of screening;*Lung transplantation anticipated in the 12 months after the start of screening;*Known hypersensitivity to the active substance or any excipient of either pirfenidone or nintedanib;*Mild (Child Pugh A), moderate (Child Pugh B) or severe ( Child Pugh C) hepatic impairment;*Severe hepatic impairment, including end-stage liver disease;*Severe renal impairment, including end-stage renal disease requiring dialysis;*History or risk of gastrointestinal (GI) tract perforation;*History of unstable or deteriorating cardiac or pulmonary disease in the 6 months before the start of screening;*Electrocardiogram (ECG) with a heart-rate*corrected QT interval * 500 milliseconds (ms) at screening, or a family or personal history of long QT syndrome;*Bleeding risk: genetic predisposition to bleeding, a haemorrhagic event in the 12 months before the start of screening, or abnormal laboratory coagulation parameters. Patients who require fibrinolysis, full-dose therapeutic anticoagulation, high-dose antiplatelet therapy, or other therapy that may substantially increase bleeding risk are excluded;*Use of strong CYP1A2 inhibitors, inhibitors ofP-glycoprotein or CYP3A4 or their inducers in the 28 days before the

start of screening ;*History of alcohol or substance abuse in the 2 years before the start of screening;*Use of any tobacco product in the 12 weeks before the start of screening, or an unwillingness to abstain from their use through the final Follow-up Visit

# Study design

## Design

| | |
|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 29-06-2016 |
| Enrollment: | 8 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Esbriet |
| Generic name: | pirfenidon |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Ofev |
| Generic name: | nintedanib |
| Registration: | Yes - NL intended use |

# Ethics review

Approved WMO

| | |
|---|---|
| Date: | 19-01-2016 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 29-04-2016 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 15-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-09-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 17-10-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 15-11-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-003280-11-NL |
| ClinicalTrials.gov | NCT02598193 |
| CCMO | NL56115.078.15 |